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10/553,111	11/06/2006	John Wilbraham Lester	10103-030-999	1893

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EXAMINER	
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ART UNIT	PAPER NUMBER
1627	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,111	LESTER ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,30 and 31* is/are pending in the application.

4a) Of the above claim(s) *5,6 and 23-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7-22, and 30-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

This Office Action is in response to the amendment submitted on 01/07/10. Claims 1-28 and 30-31 are currently pending in the application, with claims 5-6 and **23**-28 having being withdrawn and claim 29 having being cancelled. Additionally, the Examiner respectfully points out that while claim 23 was listed as being examined, because of the restriction requirement, claim 23 was in fact withdrawn. Moreover, the Office Action dated 7/7/2009 on pg. 3 further support such notion as claim 23 was not listed under the 35 U.S.C. 103(a) rejection. As a result, the Examiner maintains that claim 23 is withdrawn due to the election restriction requirement dated 10/28/08. Accordingly, claims 1-4, 7-22, and 30-31 are being examined on the merits herein.

Receipt of the aforementioned amended claims is acknowledged and has been entered.

1. Applicant's argument with respect to the rejection of claims 1-4, 7-22, and 30-31 under 35 U.S.C. 103(a) has been fully considered. Applicant argues that administration of a compound of formula I in an amount of 0.5 to 4 mg/kg/day allows for the treatment of angiotensin II related disease without affecting cortisol levels. Such arguments are however not found persuasive as applicant is arguing the amended claims. While applicant refers to figure 1b as unexpected result, the Examiner contends that such figure does not provide evidence of unexpected result or that cortisol is not affected. In

fact, Figure 1b demonstrated results involving aldosterone levels contrary to applicant's arguments (see Applicant's figure 1b). Moreover, the Examiner contends that Jones teaches the use of the metabolite and trilostane at various dosages including at about 30 mg and at lower unit dose levels such as below 100 mg (see pg. 2, lines 44-45 and 51 and pg. 13, claim 22). Such teaching does indeed render obvious applicant's newly amended claims of administration of 0.5 to 4 mg. Moreover, the Examiner contends that because Jones teaches the use of lower dosage units, determining the optimum concentration or range is well within the purview of the skilled artisan and one of ordinary skill in the art would have found it obvious to vary the concentration below 100 mg or about 30 mg as taught by Jones in order to provide the most effective amount in the treatment of diseases.

2. As for Young, it was provided to demonstrate that aldosterone is known in the art to cause various cardiovascular effects including cardiac fibrosis (i.e. cardiofibrosis). Consequently, treatments utilizing targets that inhibit aldosterone such as the compounds of Jones, would have been obvious to one of ordinary skill in the art since such compounds would be effective in treating cardiofibrosis. Consequently, the Examiner maintains that Jones in view Young does indeed render obvious applicant's invention.

For the foregoing reasons, the rejection of record remains proper and is maintained. However, in view of applicant's amendment, the following modified 103 (a) Final rejection is being made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

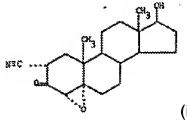
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7-22, and 30-31 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Jones et al. (GB 2 155 018 A, previously cited) in view of Young et al. (Journal of Clinical Investigation, June 1994, pgs. 2578-2583, previously cited).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Jones et al. teach 2-cyano steroid compounds for inhibiting adrenal steroidogenesis (see abstract). Particularly, Jones et al. teach that the compound of formula III is a metabolite of trilostane, which has the following structure:



(instant claims 1-3; see pg. 1, lines 8-19). Additionally, Jones et al. teach that trilostane and related compounds possess adrenocortical inhibiting properties (see pg. 1, lines 20-24). Jones et al. further teach that the compound of formula III is more potent *in vitro* than trilostane thereby suggesting that trilostane is just as effective as its metabolite (see pg. 2, lines 4-7). Additionally, Jones et al. teach that the pharmaceutical composition comprising 2-cyano steroids can be optionally combined with other active compounds and can include one or more pharmaceutically acceptable carriers or excipients (instant claims 22 and 30; see pg. 2, lines 27-29). The compositions may be presented as a tablet, a capsule, granulate or suspension (instant claim 18; see pg. 2, lines 37-39). In unit dosage forms, the composition can comprise a trilostane from about 30 to about 250 mg or at lower unit dose levels below about 100 mg (instant claims 7, 12, and 19-21; see pg. 2, lines 44-51). Trilostane and 2-cyano compounds are also taught by Jones to be effective when administered as a compound in particulate form consisting of particles having a

mean equivalent sphere volume diameter of less than 20 microns, at least 95% of the particles having a particle size of less than about 50 microns and a specific surface area of about 2 m2g-1 or higher or preferably about 2 to about 5 m2g-1 (instant claims 13-17; see pg. 2, lines 52-62). Importantly, Jones et al. teach that such compounds can be used in the treatment of adrenal cortical hyperfunction as in hypercortisolism and primary adlosteronism (see pg. 2, line 65 and pg. 3, line 1).

Jones et al. do not specifically teach the use of trilostane in his invention. Likewise Jones et al. do not teach treatment of cardiofibrosis or cardiofibrosis following infarction using trilostane. Additionally, Jones et al. do not teach administration in an amount of from 0.5 to 4 mg/kg/day.

However, Jones et al. does teach that the compounds of his invention are in effect metabolites of trilostane. Consequently, the Examiner contends that it would have been well within the purview of the skilled artisan to try trilostane since both trilostane and its metabolites are expected to be equally effective. Moreover, the Examiner contends that one of ordinary skill in the art would have found it obvious to vary the concentration below 100 mg or about 30 mg as taught by Jones during routine experimentation if the desire is to provide the most effective amount in the treatment of diseases.

Young et al. teach that aldosterone has been shown to cause various cardiovascular effects (see pg. 2578, left col. last line and right col. line 1). In fact, studies by Brilla and Weber demonstrated that rats infused with aldosterone developed hypertension and interstitial cardiac fibrosis (instant claims 4, 8-11, and 31; see right col., last paragraph). Particularly, Young et al. demonstrated that treatment with the mineralcorticosteroids aldosterone and deoxycorticosterone led to increased systolic BP and caused considerable cardiac hypertrophy (see abstract). Additionally, aldosterone treatment caused marked ventricular interstitial collagen and further confirmed that aldosterone treatment was more potent in causing cardiac fibrosis perhaps due to its effect on cardiac fibroblasts (see pg. 2580, right col., Discussion Section paragraphs 1-3).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to try trilostane for inhibiting aldosterone as Young et al. suggest that mineralcorticoids including aldosterone cause cardiac fibrosis (i.e. cardiofibrosis) and in view of Jones who teach that compounds of formula III and trilostane are effective in inhibiting aldosterone. Additionally, one of ordinary skill in the art would have found it obvious to utilize trilostane instead of its metabolite given that that both the metabolites and trilostane are taught by Jones et al. to be effective. Moreover, one of ordinary skill in the art would have found it obvious to utilize the trilostane either before or after infarction given that Young et al. demonstrated that mineralcorticoids play a role in the development of cardiofibrosis. Thus, given the teachings of Jones and Young, one of ordinary skill would have been motivated to try trilostane for the treatment of

cardiofibrosis with the reasonable expectation of providing a method that is effective in treating cardiofibrosis and a method effective in reducing systolic blood pressure.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1627

03/22/2010

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627